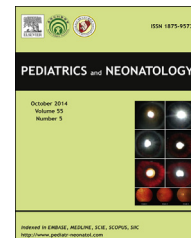


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CASE REPORT

Subcutaneous Fat Necrosis of the Newborn: Report of Five Cases

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Key Words

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Subcutaneous fat necrosis of the newborn (SCFN) is a rare, self-limited disorder of the panniculus which appears in the first few weeks of life. SCFN generally follows an uncomplicated course. However, there are important complications for which the patient must be regularly monitored, including thrombocytopenia, hypoglycemia, hypertriglyceridemia, and most importantly, hypercalcemia. We report five infants with SCFN. All children were born at term. The onset of lesions was between 1 day and 20 days after birth. The back was the most frequent location. Birth hypoxia was the most frequent risk factor. Complications included hypercalcemia, hypoglycemia, and metastatic calcifications (disseminated subcutaneous calcifications, nephrocalcinosis, and myocardial calcifications). This study provides the first case of SCFN in the context of hypoxic encephalopathy and refractory septic shock that required extracorporeal membrane oxygenation (ECMO).

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1. Introduction

Subcutaneous fat necrosis of the newborn (SCFN) is a transient panniculitis which is typically presented in neonates within the first 6 weeks of life.¹ It is characterized by

indurated, erythematous nodules, and plaques over bony prominences such as the back, arms, buttocks, thighs, and cheeks.² The prognosis is generally good and usually only symptomatic treatment is required.³ However, there are rare and serious complications for which the patient must be regularly monitored, especially hypercalcemia.² Metastatic calcifications due to prolonged hypercalcemia have been reported in isolated cases.⁴ Five of our patients were monitored in order to evaluate the risk factors, clinical aspects, and variable outcomes in relation to SCNF. Most

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reports focused on one neonate while there are only three that included more than five cases. To the best of our knowledge, only one previous case of a neonate with myocardial calcifications has been reported in the literature.⁵

2. Case reports

We retrospectively analyzed five infants with SCFN, three boys and two girls, who were diagnosed in a tertiary pediatric hospital from 1995 to 2013 (Table 1). All infants were born at term (range 37–41 weeks). The mean age of the mothers at the time of delivery was 30 years (range 25–33 years). One mother had gestational diabetes and the others had uncomplicated pregnancies. Three neonates were delivered by emergency cesarean section because of fetal distress and one infant required forceps delivery. Four out of five (80%) children had normal birth weight and only one was macrosomic. Except for one case, most of the neonates showed birth asphyxia in the context of sepsis, anemia, esophageal atresia, and meningitis. The median 1–5 minutes Apgar score was 3.6–6.6. Therapeutic hypothermia and extracorporeal membrane oxygenation (ECMO) were required in one infant with hypoxic encephalopathy due to refractory septic shock and cardiorespiratory arrest (CRA). The skin lesions appeared a mean of 8 days (range 1–20 days) after delivery, as indurated, erythematous



Figure 1 Skin lesions caused by subcutaneous fat necrosis of one of the infants: erythematous plaques and nodules on the back.

nodules and plaques. The first three cases had localized lesions with fewer than four nodules while Patient 4 and Patient 5 developed diffuse lesions. The most common locations were the back followed by the arms (Figure 1). The diagnosis was made on the basis of clinical features and confirmed by skin biopsy. Histopathologically, all cases showed fat cell necrosis with a dense inflammatory infiltrate composed of lymphocytes, histiocytes, and

Table 1 Subcutaneous fat necrosis of the newborn: evaluation of risk factors, clinical manifestations, and complications.

Patient/ sex	Term (wk)	Labor	Maternal age/ history	Birth weight (g)	Apgar (1–5 min)	Perinatal course	Onset/ resolution (d)	Site	L or D/mm	Complications
1/male	39	ECS	32/No	3520	5–7	Birth asphyxia, esophageal atresia	20/60	Back	L*/12 × 16	None
2/female	38	Vaginal	30/No	3200	8–9	None	1/90	Back	L/8 × 8	None
3/female	41	Vaginal (forceps)	29/No	3350	5–9	Asphyxia, meconium aspiration	2/90	Neck, Back, buttocks groin	L/20 × 30	Asymptomatic hypercalcemia
4/male	40	ECS	33/No	3820	0–4–7	Distress fetal, hypoxic encephalopathy, therapeutic hypothermia, ECMO, sepsis, anemia, ARF, sinus thrombosis, CRA	12/90	Back, arms	D†	Symptomatic hypercalcemia (hypertension, vomiting, lethargy), hypoglycemia
5/male	37	ECS	25/ Diabetes	3770	0–4	Hypoglycemia, sepsis, hypertrophic cardiomyopathy, cerebral palsy, meningitis, hypocalcemia, ARF	6/150	Arms, legs	D	Hypercalcemia, nephrocalcinosis, myocardial calcification, disseminated subcutaneous calcifications

ARF = acute renal failure; CRA = cardiorespiratory arrest; D = diffuse; ECMO = extracorporeal membrane oxygenation; ECS = emergency cesarean section; L = localized; N = normal; NK = not known.

* Fewer than four nodules.

† Four or more nodules.

multinucleated giant cells. Some lipocytes were replaced by radially arranged needle-shaped clefts and, at a later stage, areas of calcification were found within the fat.

According to our follow up, the skin lesions on all infants resolved spontaneously within a mean of 3.2 months (range 2–5 months). Patients with localized SCFN did not develop any complications except for Patient 3, who had asymptomatic hypercalcemia 39 days after delivery (11.9 mg/dL), but the rates normalized after 1 month (8.4 mg/dL). Patients with diffuse lesions developed symptomatic hypercalcemia. Patient 4 had vomiting and was agitated. Laboratory analysis on postnatal Day 30 revealed a serum calcium level of 16 mg/dL, with a phosphorus level of 5.2 mg/dL. For treatment, the patient received low calcium and vitamin D formula, hyperhydration, intravenous methylprednisolone at a dose of 2 mg/kg/day, and furosemide (4 mg/kg/day). Due to a lack of response, we started treatment with oral etidronate (10 mg/kg/day) for 7 days to normalize his serum calcium level (8.8 mg/dL). The patient was discharged and underwent periodic calcium checkups. Patient 5 was referred from another hospital with the diagnosis of SCFN and delivery complications as detailed in Table 1. Echocardiogram depicted echodense lesions in the septum and the right ventricular free wall, which were diagnosed as calcifications. On the radiography, there were calcium deposits in the soft tissues of extremities corresponding to previous areas of SCFN (Figure 2). A renal ultrasound revealed renal parenchyma calcifications on Patient 5, who was 15 years old and receiving annual checks that showed the same findings, without affecting myocardial or renal function.

3. Discussion

SCFN is a rare type of localized lobular panniculitis which is usually found in full–post-term infants.⁵ The pathogenesis of SCFN remains unclear. It has been postulated that any neonatal distress may interfere with normal blood supply to the fat tissue, creating an environment of hypoxia and hypothermia, which is believed to lead to inflammation and

necrosis. In addition, the hypodermis of the newborn has a higher proportion of saturated fats (i.e., stearic and palmitic acids), which have a higher melting point (64 °C) making them more likely to crystallize under colder conditions.²

Possible neonatal risk factors include perinatal asphyxia, meconium aspiration, cord accidents, hypothermia, hypoglycemia, anemia, thrombocytosis, and lactic acidosis. Maternal associations include preeclampsia, hypertension, gestational diabetes, cocaine or cigarette exposure, calcium blocker use during pregnancy, and familial dyslipidemia. Traumatic birth and contact with cold surfaces are the local causes.^{4,6} In our patients, birth asphyxia was the most commonly identified predisposing factor.

Additionally, early cases of SCFN were documented in neonates who underwent whole-body cooling prior to being placed on cardiopulmonary bypass and therapeutic moderate hypothermia for newborns with hypoxic-ischemic encephalopathy.^{7,8} Patient 5 highlights the fact that induced whole-body cooling for hypoxic-ischemic encephalopathy may play a role in the development of SCFN. He was also connected to ECMO due to refractory septic shock and CRA. These factors could precipitate SCFN by causing decreased tissue perfusion with relative hypoxia and hypothermia.

SCFN generally follows an uncomplicated course with spontaneous resolution over several weeks. However, there are rare and serious complications for which the patient must be regularly monitored including thrombocytopenia, hypoglycemia, hypertriglyceridemia, and most importantly hypercalcemia.² Hypoglycemia and thrombocytopenia precede the development of SCFN in infants with perinatal hypoxia, which might suggest that they are most likely caused by hypoxia injury. In Patient 5, hypoglycemia was found 10 days before skin lesions appeared and this could be due to birth asphyxia. Hypercalcemia is not common, but it is one of the most dangerous complications.⁹ Although hypercalcemia generally manifests with the onset of skin lesions, it has been reported to occur as late as 6 months afterwards, which is why patients with SCFN warrant long term follow up of their serum calcium levels.³ Untreated

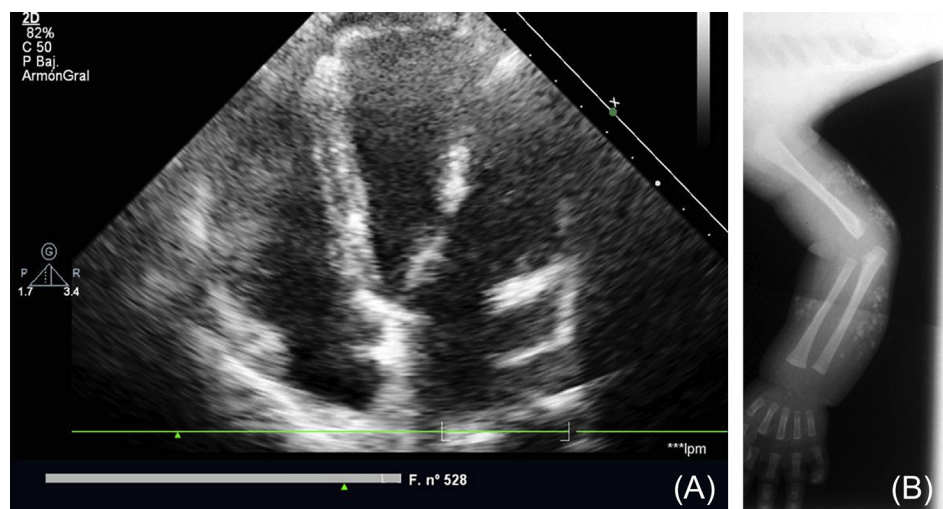


Figure 2 (A) Echocardiographic apical four chamber view of the heart: echodense lesions in septum and right ventricular free wall; (B) X-rays of both legs show calcifications in the soft tissue corresponding to previous areas of subcutaneous fat necrosis of the newborn (SCFN).

hypercalcemia may lead to severe complications, both acute, like cardiac arrest and renal failure, as well as chronic problems, such as metastatic calcifications. Metastatic calcifications have been reported to be rarely found in kidneys, falx cerebri, skin, myocardium, liver, inferior vena cava, and gastric mucosa.^{2,4,5,7} Patient 5 was admitted with extensive metastatic calcifications. It was impossible to know the severity or the duration of his hypercalcemia, because he had been transferred from another hospital. The pathogenesis of hypercalcemia is not fully understood.¹⁰ The most widely accepted theory proposes that the elevated 1,25-Hydroxyvitamin D3 secreted from the granulomas of the skin lesions can stimulate intestinal calcium uptake.² A correlation between the extension of SFCN and the presence of truncal lesions with hypercalcemia was noted by Mahé et al.⁶ This correlation was also found in our patients.

The differential diagnoses including sclerema neonatorum, hemangioma, cellulitis, histiocytosis, erythema nodosum, Faber disease, fibromatoses, and rhabdomyosarcomas are all histologically different.¹¹ Histopathologically, SCFN shows necrosis of the fat, abundant histiocytes, multinucleated giant cells with granuloma formation, and lipocytes with radially arranged needle-shaped clefts that are doubly refractile under polarized light microscopy.²

In summary, a neonate who develops skin lesions consistent with SCFN should be followed up for the possible onset of hypoglycemia, thrombocytopenia, hypertriglyceridemia, and especially hypercalcemia. This study provides the first case of SCFN in the context of a refractory septic shock that required ECMO. It also represents variable clinical courses ranging from localized lesions of SCFN to diffused forms that developed symptomatic hypercalcemia and metastatic calcifications.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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